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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/423,259 03/02/00 HANNI

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EXAMINER

EINSMANN, J	
ART UNIT	PAPER NUMBER

1655

DATE MAILED:

05/17/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.

09/423,259

Applicant(s)

HANNI ET AL.

Examiner

Juliet C. Einsmann

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 06 March 2001.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 17-27 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 17-27 is/are rejected.
- 7) ☒ Claim(s) 20 and 24 is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

- 15) ☐ Notice of References Cited (PTO-892)
- 16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 18) ☐ Interview Summary (PTO-413) Paper No(s) _____
- 19) ☐ Notice of Informal Patent Application (PTO-152)
- 20) ☒ Other: English language translation: Foreign

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DETAILED ACTION

1. This action is written in response applicant's correspondence submitted 3/6/01, paper number 15. Claims 1-16 have been canceled and claims 17-27 have been added. Claims 17-27 are pending. Applicant's amendments and arguments have been thoroughly reviewed, but are not persuasive for the reasons that follow. Any rejections not reiterated in this action have been withdrawn. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. **This action is FINAL.**

NEW GROUNDS OF REJECTION AND OBJECTION NECESSITATED BY APPLICANT'S AMENDMENT OF THE CLAIMS

Claim Objections

2. Claim 24 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Claim 24 is drawn to probes comprising the oligonucleotides of claim 23. The oligonucleotides of claim 23 are drawn using closed "consisting of" language. Therefore, the use of "comprising" language in claim 24 broadens the scope of the base claim from which it depends. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

3. Claim 20 would be allowable if rewritten to overcome the rejection(s) under 35 U.S.C. 112, second paragraph, set forth in this Office action and to include all of the limitations of the base claim and any intervening claims.

Claim Rejections - 35 USC § 112

4. Claims 19, 20, 22, and 24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 19 and 20 are indefinite over the language "and one SEQ ID NO: 4, SEQ ID NO: 5, and SEQ ID NO: 6" because this language is unclear. Amendment to include the word "of," for example "and one of SEQ ID NO: 4" would obviate this rejection.

Claim 22 is indefinite because it recites "pairs of oligonucleotide primers according to claim 21," but then claim 22 includes SEQ ID NOs not encompassed by the primer pairs of claim 21. This is unclear.

Claim 24 is indefinite over the recitation of "complementary or inverse/complementary" because it is not clear what is meant by this language. It is not clear what is meant by inverse/complement. For example, given the sequence 5'-CAT-3', the complement is 3'-GTA-5' or 5'-ATG-3'. Is the inverse complement then 5'-GTA-3'?

Claim Rejections - 35 USC § 102

5. Claim 24 is rejected under 35 U.S.C. 102(b) as being anticipated by Loftus *et al.* (PNAS USA Vol. 91, pp. 2757-2761, March 1994).

Loftus *et al.* teach oligonucleotides which comprise mtDNA from representative breeds of cattle. Loftus *et al.* teach many different sequences which are fully disclosed as GenBank

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accession numbers L27712-L7737 (p. 2757). These sequences comprise the instantly claimed sequences.

Instant SEQ ID NO: 8 consists of nucleotides 225-705 of the sequence disclosed in GenBank Accession number L27725. Therefore, this sequence taught by Loftus *et al.* also comprises instant SEQ ID NO: 7 (nucleotides 310-336) and 19 (nucleotides 423-447), which are merely segments of SEQ ID NO: 8.

The instantly rejected claim is drawn to probes which comprise the oligonucleotides according to claim 23- that is instant SEQ ID NO: 7 and SEQ ID NO: 19. The sequence taught by Loftus *et al.* comprises both SEQ ID NO: 7 and SEQ ID NO: 19, and therefore the teachings of Loftus *et al.* meet the limitations of the instant claim.

Claim Rejections - 35 USC § 103

6. Claims 17-19, 21-23 and 25-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Loftus *et al.* (PNAS USA, Vol. 91, pp. 2757-2761, March 1994) in view of Fei *et al.* (Animal Science and Technology (1996) Vol. 67, No. 10, pp. 900-905).

Loftus *et al.* teach the sequences of the D loops of the mtDNA from a number of cattle breeds. These sequences are fully disclosed in GenBank accession numbers L27712-27737. Instant SEQ ID NO: 2 consists of the complement of nucleotides 685-699 of the sequence disclosed in GenBank Accession number L27725 (see attached GenBank record). Instant SEQ ID NO: 5 consists of nucleotides 230-244 of the sequence disclosed in GenBank Accession number L27725.

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Furthermore, the sequence taught by Loftus *et al.* and fully disclosed in GenBank accession number L27725 also comprises instant SEQ ID NO: 9-14. Instant SEQ ID NO: 9 consists of nucleotides 19-43, instant SEQ ID NO: 10 consists of the complement of nucleotides 158-177, instant SEQ ID NO: 11 consists of the complement of nucleotides 358-377, instant SEQ ID NO: 12 consists of nucleotides 441-60, instant SEQ ID NO: 13 consists of nucleotides 715-734, and instant SEQ ID NO: 14 consists of the complement of nucleotides 854-873.

Instant SEQ ID NO: 8 consists of nucleotides 225-705 of the sequence disclosed in GenBank Accession number L27725. Therefore, this sequence taught by Loftus *et al.* also comprises instant SEQ ID NO: 7 (nucleotides 310-336) and 19 (nucleotides 423-447), which are merely segments of SEQ ID NO: 8.

Instant SEQ ID NO: 15 consists of nucleotides 15824-15981 of the sequence disclosed in GenBank Accession number L27725.

Instant SEQ ID NO: 16 consists of nucleotides 225-337 of the sequence disclosed in GenBank Accession number L27725.

Instant SEQ ID NO: 17 consists of nucleotides 441-705 of the sequence disclosed in GenBank Accession number L27725.

Instant SEQ ID NO: 18 consists of nucleotides 745-902 of the sequence disclosed in GenBank Accession number L27712 (see attached GenBank record).

Loftus *et al.* do not teach nucleic acids which consist of the instantly claimed nucleic acids, nor do they teach primer pairs which comprise oligonucleotides that consist of the instantly disclosed sequences.

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Fei *et al.* teach methods for specific identification of meat from cattle using the PCR with primers designed to amplify portions of the mitochondrial D-loop DNA sequence (p. 900-905). Primer BF taught by Fei *et al.* consists of nucleotides 397-416 of the sequence taught by Loftus *et al.* The primer taught by Fei *et al.* is considered to be a functional homologue of all of the primers and probes of the instantly claimed invention, since the primer disclosed by Fei *et al.* possesses the same function as those of the instant invention, namely to amplify and/or detect portions of the D loop mtDNA from cattle.

In light of the sequences taught by Loftus *et al.* and the teaching by Fei *et al.* that beef samples can be specifically identified by PCR amplification of the D-loop of mitochondrial DNA, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have selected any primers from the sequences taught by Loftus *et al.* in order to have provided functional homologues of the primers taught by Fei *et al.* The selection of different primer pairs from the sequences taught by Loftus *et al.* would have provided the ordinary practitioner with additional mechanisms for the specific amplification and detection of D-loop mitochondrial DNA from beef products in meat samples. The ordinary practitioner would have had a more than reasonable expectation of success since Fei *et al.* teach that amplification with primers specific for the D-loop mtDNA of cattle results in the ability to detect small amounts of beef in a mixed meat sample, for example 0.1% of beef in pork.

Response to Remarks

Applicant provides several lines of argument to support the patentability of the instant claims in view of the prior art. These arguments have been carefully considered, but are not found to be persuasive for the reasons that follow.

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Applicant argues that the claimed oligonucleotides are unobvious because the nucleic acids claimed have the specific properties of being specific to bovines and the ability to amplify all bovine breeds, whatever their geographic origin. A careful review of the specification identified that these unexpected results have been shown with regard to only the primers disclosed as SEQ ID NO: 3 and 6. These primers are not rejected above, and their patentability is discussed in the "Allowable Subject Matter" section below. With regard to the other nucleic acids this argument is not persuasive because applicant has not provided evidence of the unexpected result that these claimed probes and primers have the properties asserted by applicant. Arguments of counsel are not found to be persuasive in the absence of a factual showing. MPEP 716.01(c) makes clear that

"The arguments of counsel cannot take the place of evidence in the record. In re Schulze , 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965). Examples of attorney statements which are not evidence and which must be supported by an appropriate affidavit or declaration include statements regarding unexpected results, commercial success, solution of a long - felt need, inoperability of the prior art, invention before the date of the reference, and allegations that the author(s) of the prior art derived the disclosed subject matter from the applicant."

Applicant provides further arguments regarding the fact that the primers of the instant invention amplify products of a certain size, are usable together, and would hybridize to the target DNA in optimal conditions. Each of these characteristics of the primers are considered matters of experimental choice, which are routinely optimized by practitioners to achieve the desired result. As noted in *In re Aller*, 105 USPQ 233 at 235, "More particularly, where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." Routine optimization is not considered inventive and no evidence has been presented that the probe selection performed was

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other than routine, that the products resulting from the optimization have any unexpected properties, or that the results should be considered unexpected in any way as compared to the closest prior art.

Applicant provides arguments that a number of oligonucleotide sequences derived from the Loftus *et al.* disclosure would not have the unexpected properties of being specific for bovines and not other species and/or being able to amplify DNA from all bovines. The examiner does not argue against this assertion, but points out that these sequences would in fact have the expected property of being able to amplify the D-loop of mitochondrial DNA. These claims are in fact product claims and not method claims, and thus the nucleic acids that are obviated by the combined teachings of Loftus *et al.* in view of Fei *et al.* do not necessarily have to function in the methods disclosed in the instant application. As discussed in the rejection above, the prior art provides ample motivation and teaching to lead the ordinary practitioner to smaller probes and primers derived from the sequence taught by Loftus *et al.* The products obviated by the teachings of Loftus *et al.* in view of Fei *et al.*, and indeed the examples provided in applicant's arguments, would have the ability to amplify and/or detect D-loop mtDNA from some bovines if not every bovine. Furthermore, it is noted that some of the claimed oligonucleotides are in fact probes of longer length than the claimed primers. These probes are also considered functional homologues of the nucleic acids taught by Loftus *et al.* in view of Fei *et al.* since they certainly would have the ability to detect bovine mtDNA.

Applicant points out that it is possible to obtain patents to smaller DNA fragments of previously disclosed sequences, citing issued patent US 5596089. The examiner does not argue that such issuance is possible, and in fact has designated some of the subject matter of the instant

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application allowable. However, every case must be examined on its own merits, and prior to the allowance of any claims patentability must be determined. The instantly rejected claims are considered obvious for the reasons discussed above.

With regard to SEQ ID NO: 2 and 5, these nucleic acids are smaller portions of allowable SEQ ID NO: 3 and 6. The unexpected results with regard to SEQ ID NO: 3 and 6 are not considered to apply to the shorter sequences because the specificity of SEQ ID NO: 3 and 6 is so largely dependent on the length of the probe. Absent some evidence that SEQ ID NO: 2 or 5 have the same unexpected property of SEQ ID NO: 3 and 6 these oligonucleotides are considered obvious over the prior art. These same comments would apply to oligonucleotides consisting of 15 to 25 nucleotides of SEQ ID NO: 1 or SEQ ID NO: 4.

Allowable Subject Matter

7. The following is a statement of allowable subject matter as well as reasons for the indication of allowable subject matter: Claims which require the presence of nucleic acids consisting of SEQ ID NO: 3 or consisting of SEQ ID NO: 6 are unobvious over the prior art. While the prior art provides longer sequences which comprise SEQ ID NO: 3 and SEQ ID NO: 6, and the prior art provides motivation to design primers for the amplification of bovine mtDNA, this teaching is not sufficient to obviate nucleic acids which consist of SEQ ID NO: 3 or SEQ ID NO: 6. These nucleic acids are considered to be unobvious in light of the unexpected results provided in the specification, wherein these nucleic acids are shown to amplify bovine mtDNA but not that of horse, sheep, pig, duck, chicken or turkey (Figure 1). Further, nucleic

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acids consisting of SEQ ID NO: 3 and SEQ ID NO: 6 are shown to amplify mtDNA from many different breeds (Figure 2).

8. Nucleic acids consisting of SEQ ID NO: 1 and SEQ ID NO: 4 are also unobvious over the prior art of record because these nucleic acids comprise SEQ ID NO: 3 and SEQ ID NO: 6. It is assumed that, although slightly longer, these nucleic acids would function as primers with the same level of specificity as SEQ ID NO: 3 and SEQ ID NO: 6.

Conclusion

9. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Enclosed with this action, for applicant's convenience is a copy of the English language translation of the entirety of the Fei *et al.* reference.

10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

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11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Juliet C. Einsmann whose telephone number is (703) 306-5824. The examiner can normally be reached on Monday through Thursday, 7:00 AM to 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones can be reached on (703) 308-1152. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 and (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.



JEFFREY FREDMAN
PRIMARY EXAMINER



Juliet C. Einsmann
Examiner
Art Unit 1655

May 10, 2001